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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,162	08/29/2006	Kornelia Polyak	00530-116US1 DFCI 853.02	5286
26161 7590 01/27/2010 FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER SWITZER, JULIET CAROLINE	
			ART UNIT 1634	PAPER NUMBER
			NOTIFICATION DATE 01/27/2010	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No. 10/550,162	Applicant(s) POLYAK ET AL.	
	Examiner Juliet C. Switzer	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,8-23,26,32,40,50,51,58,64,71,72 and 79 is/are pending in the application.
- 4a) Of the above claim(s) 1,2,9-23,26,32,40,50,51,58,64,71 and 72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8 and 79 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1634

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 8 and 79 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The full text of the rejection is given beginning on page 3 of the office action mailed 7/17/09. The portion of the rejection referring to non-human organisms is moot in view of the amendments to the claims.

Response to Remarks

The response states that “Where a gene is expressed in cancer cells of various stages and grades but not in normal cells, a strong possibility is that the expression of the gene increases with the degree of advancement of the cancer.” This attorney argument is contraindicated by Ma et al. who teach that the pathologically discrete stages (ADH, DCIS, and IDC) of breast cancer are highly similar to each other at the level of the transcriptome. They further teach that this finding supports the idea that the distinct stages of progression are evolutionary products of the same clonal origin, and that genes conferring invasive growth are active in the preinvasive stages. Following this teaching, it was highly unpredictable at the time the invention was made whether or not any quantifiable difference existed between CTSK levels in samples from

Art Unit: 1634

different stages of cancer. Further, as noted in the rejection Littlewood-Evans had attempted to demonstrate difference in gene expression of CTSK in DCIS versus invasive tumors and failed.

Applicant points to portions of the specification that would have "persuaded" one having skill in the art that CTSK would be differentially expressed in DCIS and invasive breast cancer. These portions of the specification include statements that CTSK could be used as claimed and showings that other genes are differentially expressed in these types of cancer. On page 74 of the specification, the specification teaches that "The expression of no single gene was found to distinguish between DCIS and invasive tumors," which would not have lead one having skill in the art to believe that the claimed methods would be functional. This statement suggests that finding genes that are differentially expressed between two phenotypes is not even sufficient to identify genes that will be successfully used in single gene classification schemes. Further, prior to the instant invention, Littlewood-Evans had attempted to demonstrate difference in gene expression of CTSK in DCIS versus invasive tumors and failed.

Applicant argues that the methods for testing for relative levels of gene expression are straight forward, and that there are a small number of genes to test listed on page 123. However, the genes listed on page 123 are not the only genes the specification discusses or suggests may be useful in such an assay- there are hundreds of such genes listed in the various tables (see page 22-23 which states any of the genes in tables 1-16 are useful for distinguishing). For CTSK in particular, prior art evidence has been given to support that the functionality of the method would have been highly unpredictable.

Applicant provides a post-filing date reference, namely Kleer et al. to demonstrate that the skilled artisan would have been correct in his or her reasonable belief, as of the filing date of

Art Unit: 1634

the application in the differential expression of CTSK gene by DCIS and invasive breast cancer. The Kleer et al. paper has been considered to the extent that the facts contained therein might be convincing, but it is noted that a publication cannot substitute for expert testimony, and is not considered a proper declaration. "The reason for requiring evidence in declaration or affidavit form is to obtain the assurances that any statements or representations made are correct, as provided by 35 U.S.C. 25 and 18 U.S.C. 1001." Permitting a publication to substitute for expert testimony would circumvent the guarantees built into the statute. *Ex parte Gray*, 10 USPQ2d 1922, 1928 (Bd. Pat. App. & Inter. 1989). (see MPEP 716.02(g)).

Even if the paper were given in declaration form the paper does not establish that the specification was enabling at the time that it was filed. Evidence to supplement a specification which on its face appears deficient under 35 U.S.C. 112 must establish that the information which must be read into the specification to make it complete would have been known to those of ordinary skill in the art, and affidavits or declarations presented to show that the disclosure of an application is sufficient to one skilled in the art are not acceptable to establish facts which the specification itself should recite (MPEP 716.09 and 2164.05). Here applicant argues that the further experimentation presented in the Kleer et al. paper would have been appropriate "routine experimentation" but applicant does not establish that the information which must be read into the specification would have been known to those of ordinary skill in the art, as the "information" had not yet been established.

The reference does not address the high degree of unpredictability demonstrated in the prior art and discussed in the rejection- in particular the fact that the prior art was suggestive that the claimed method would not function since Littlewood-Evans had attempted to demonstrate

Art Unit: 1634

difference in gene expression of CTSK in DCIS versus invasive tumors and failed. Further, although Kleer et al. found a difference in expression between DCIS and infiltrating ductal carcinoma (Table 1(B)) they teach that this difference does not reach statistical significance when corrected for multiple comparisons (p. 5364). Also, they do not demonstrate that the gene expression would be sufficient to actually appropriately classify individuals, as instantly claimed. As previously noted, the specification teaches that no single gene tested was successful at properly classifying individuals.

Thus, having carefully considered the arguments, the rejection is maintained.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday or Tuesday from 8:30 AM until 5:00 PM, or on

Application/Control Number: 10/550,162

Page 6

Art Unit: 1634

Wednesday from 8:00 AM until 1:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached by calling (571) 272-0731.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Art Unit: 1634

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Juliet C. Switzer/
Primary Examiner
Art Unit 1634

January 26, 2010